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Paper

EPIDEMIOLOGIC STUDIES OF PILOTS AND AIRCREW

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***Abstract*—During flight, pilots and cabin crew are exposed to increased levels of cosmic radiation which consists primarily of neutrons and gamma rays. Neutron dosimetry is not straightforward, but typical annual effective doses are estimated to range between two and five mSv. Higher dose rates are experienced at the highest altitudes and in the polar regions. Mean doses have been increasing over time as longer flights at higher altitudes have become more frequent. Because there are so few populations exposed to neutrons, studies of airline personnel are of particular interest. However, because the cumulative radiation exposure is so low, statistical power is a major concern. Further, finding an appropriate comparison group is problematic due to selection into these occupations and a number of biases are possible. For example, increased rates of breast cancer among flight attendants have been attributed to reproductive factors such as nulliparity and increased rates of melanoma among pilots have been attributed to excessive sun exposure during leisure time activities. Epidemiologic studies conducted over the last 20 y provide little consistent evidence linking cancer with radiation exposures from air travel.**

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INTRODUCTION

DURING the last 20 y, several epidemiologic studies have been conducted of pilots and cabin crew. Early studies were of military pilots who served during World War I, World War II, and the Korean conflict. Subsequent studies involved aircrew from commercial airlines but were limited because of small numbers. Ongoing studies are large and comprehensive and should provide more definitive information on possible occupational risks associated with flight (Blettner et al. 1998).

The early studies generally found that pilots were a very healthy group who lived longer than the general population. This longevity was related to selection factors associated with aviation, which required an especially healthy workforce. Not surprising, an increase in death related to airplane accidents was the most striking feature of their mortality patterns.

Epidemiologic issues in studying aircrew include the low-cumulative dose (of the order of 100 mSv) and associated low statistical power to detect a radiation effect, the availability of a valid comparison population, since aircrews possess characteristics and lifestyles that differ appreciably from the population in general, occupational risk factors other than cosmic rays, exposure assessment related to incomplete historical flying records, and whether the radiation weighting factors (w_R) used to compute millisievert values for neutrons for radiation protection purposes are applicable for biological endpoints in humans such as cancer induction (CIRRPC 1995; NCRP 1995).

SOURCES OF RADIATION EXPOSURE

Pilots and aircrew are exposed to cosmic radiation, which consists primarily of high-LET neutrons and low-LET gamma rays. At high altitudes, about half the effective dose would be due to neutrons. The neutrons are created from secondary interactions when high-energy protons from space smash into air molecules in the upper atmosphere. The energy distribution of the neutrons is complex, and their relative biological effectiveness compared to low-LET radiation in causing human cancers is not known. Levels of cosmic radiation increase with altitude because of the loss of the shielding effect of Earth's atmosphere. Levels also vary with latitude, being highest near the poles where Earth's magnetic field provides less shielding. There are also defects in Earth's magnetic field, such as the south Atlantic anomaly, associated with higher radiation levels. Solar flares are another source of radiation exposure; although rare, solar events can be associated with a high-exposure rate. Finally, any radioactive cargo could contribute to total radiation exposure, although this source is thought to be minimal overall.

ATTENTION AND AWARENESS

A renewed attention and awareness of cosmic radiation became focused in 1991 when the International

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Commission on Radiological Protection (ICRP) published their recommendation that natural sources of radiation should be incorporated into occupational exposures for aircrew. Specifically "...the Commission recommends that there should be a requirement to include exposures to natural sources as part of occupational exposure only in the following cases: ... (c) operation of jet aircraft ... case (c) will relate principally to the aircraft crew, but attention should also be paid to groups such as couriers who fly more often than other passengers" (ICRP 1991). The ICRP also recommended that occupational exposures be limited to 20 mSv y^{-1} and that the limit for the general population be lowered to 1 mSv y^{-1}. It was further recommended that pregnancy, once declared, should receive special exposure restrictions to ensure that the fetus does not receive greater than 1 mSv for the remainder of the pregnancy. The ICRP recommendations in Publication 60 generated much interest with conferences on dosimetry and regulatory matters being held during the last decade (Reitz et al. 1993; International Workshop 1998).

Issues of regulating exposures and monitoring aircrews and frequent fliers have arisen (McAulay et al. 1996; Bagshaw 1998). One implication is that business travelers might be considered "radiation workers" if their annual dose exceeds 1 mSv from natural background radiation received in flight, an extremely low level. At current commercial aircraft altitudes (30,000 to 40,000 ft), cosmic-ray doses are about 5 to 8 μSv h^{-1} and perhaps 12 to 20 μSv h^{-1} at 65,000 ft (NCRP 1995). It would take about 100 h of flying per year on the Concorde to exceed 1 mSv y^{-1} and about 200 h flying at lower altitudes on transequatorial routes. Given that some transatlantic and Pacific Basin flights result in 0.06 mSv one way, it would only take about six to eight round trip flights for a business traveler or frequent flyer to be considered a radiation worker.

ESTIMATED EXPOSURE TO AIRCREW

The epidemiologic issues in assessing radiation exposure concern the hours in flight, the routes taken, the cruise altitude, the calendar period, and the accuracy of converting the neutron component to equivalent dose in millisieverts. Not all hours are equal. For example, block time relates to the "gate to gate" time and not total time in flight. Total time in flight is not necessarily sufficient for estimating cosmic-ray dose, because it takes time for planes to ascend to their cruise altitude and then time to descend, and radiation exposures would vary according to the different times at different altitudes. Routes taken and cruise altitude are even more important. For example, a polar route at an altitude of 41,000 ft by a Boeing 747-400 might result in more radiation exposure than an equator flight at very high altitudes (51,000 ft) by a Concorde.

Until recently there have been uncertainties in accurately estimating the exposure to aircrew flying at high altitudes because of the complexity of the neutron spectra. Radiation weighting factors (quality factors) also vary by neutron energy with differences related to LET characterizations. Sophisticated computer programs have been developed, however, and additional measurement experience is being acquired (UNSCEAR 1993). For example, using CARI, a program to compute estimated exposures, a pilot flying between Los Angeles and Frankfurt for 700 block hours would receive an estimated yearly average dose of 4.1 mSv (range between 3.5 to 4.7 mSv depending on solar activity). Flying for the same 700 block hours between Frankfurt and Lagos, Nigeria would result in 1.5 mSv.

Table 1. Estimates of annual radiation exposure to aircrew flying at high altitudes.

Source	mSv y^{-1}
Federal Aviation Administration (Friedberg et al. 1989; FAA 1990)	0.2–9.1
Concorde, British Airways (Bagshaw et al. 1996)	3–6
Air France (Montagne et al. 1993)	2–3
Lufthansa (Regulla and David 1993)	3–5
UNSCEAR (1993)	2.5–3.5
Australian Airlines (Wilson et al. 1994)	1–1.8
Canadian Aircrew (Tume et al. 1998)	0.7–4.2
Air Canada (Band et al. 1996)	6
Finnair Aircrew (Oksanen 1998)	1–3

Exposure assessment for pilots is reasonably good because of the completeness of flight records and the computer programs now available to account for exposures at different altitudes and latitudes. Exposure assessment for cabin crew is a bit more problematic because their flight history records are usually discarded within a few years and most aircrew fly a wide variety of routes in a given year.

When flying at high altitudes some aircrews may receive between 4 and 6 mSv y^{-1} (Table 1). Such annual doses are low and only a few times natural background. Flying for 20 or 30 y at such levels might result in a cumulative career dose of only 80 to 180 mSv, i.e., levels associated with such low risk that epidemiology would be unable to detect them. From studies of acute exposures, the relative risk (RR) of death from all cancers following 1,000 mSv is estimated to be approximately 1.6 (Pierce et al. 1996). Assuming linearity and no reduction in risk for prolonged yearly exposures, the RR estimate for 100 mSv would be 1.06 and not detectable by epidemiologic methods.

NONRADIATION FACTORS

There is an array of nonradiation factors and exposures associated with flight and a flying occupation (Table 2). Aircrew are not only exposed to cosmic rays but also to other environmental factors such as jet fuel and associated benzene components, jet engine emissions and hydrocarbon pollutants (McCartney et al. 1986), hydraulic fluids, ozone, a known mutagen (Mustafa et al. 1988), environmental tobacco smoke (Ryan 1991), electromagnetic fields and radar, and other cabin air pollutants (carbon dioxide, carbon monoxide, nitrogen oxides,

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Table 2. Non-radiation exposures and other factors associated with air travel and a flying occupation.

Occupational exposures
Jet fuel, hydraulic fluids
Jet engine emissions and combustion products
Environmental tobacco smoke
Ozone
Radar
Electromagnetic fields
Cabin air pollutants
• Carbon dioxide
• Nitrogen oxides
• Carbon monoxide
• Organic hydrocarbons
Infectious agents
Other
• Noise and vibration
• Pressure/decompression
• Relative humidity
• Temperature
Occupational factors
Irregular working hours
Disrupted sleep patterns
Chronic fatigue
Alterations of circadian rhythms
Inadequate diet
Psychological demands—job stress
Prolonged standing and lifting
Intense medical surveillance
Possible non-occupational factors
Decreased use of tobacco?
Delayed child bearing?
Increased recreational sun exposure?
High social class?
Risky hobbies/life styles?

organic hydrocarbons). Sedentary work might be a factor associated with increased rates of colorectal cancer seen among pilots in some studies. There is anecdotal evidence that pilots might smoke cigarettes to a less extent than persons in the general population and that they might receive more ultraviolet exposure from recreational activities.

Other occupational factors include irregular working hours, alteration of circadian rhythms due to flying over many time zones in short periods of time, chronic fatigue, disturbance of ovarian function, inadequate diet, and psychological demands and associated stress. For flight attendants there is the possibility of prolonged standing and lifting. In addition, there are other factors such as noise and related hearing problems, pressure/decompression and related anoxia, relative humidity and temperature changes. Further, there is an increased probability of infectious agents being spread as suggested recently following exposure to a highly infectious person with tuberculosis (Kenyon et al. 1996). Cosmic radiation, then, is not the only occupational factor of potential concern nor is cancer the only potential disease/illness that might be associated with flight. Further, pilots must undergo stringent health examinations, which selects especially healthy individuals for continued service, as well as increases the likelihood of detecting indolent diseases. Aircrew may also have lifestyles that differ appreciably from the general population emphasizing—again, the importance of an appropriate comparison group.

EARLY STUDIES

Early studies were mainly of military pilots who had flown in World War I, World War II, and the Korean conflict (MacIntyre et al. 1978; Hoiberg and Blood 1983; Hrubec et al. 1992). These studies were often part of a comprehensive surveillance of military flight personnel, and cosmic-radiation exposures were rarely mentioned. Except in special circumstances, military pilots would be unlikely to receive the same level of exposure to cosmic radiation as commercial aircrews. The early studies reported a low overall risk of death compared to the general population, reflecting the selection factors associated with a healthy workforce (Table 3). Significant deficits were seen for cardiovascular disease in particular. Lung cancer also occurred below expectation suggesting that tobacco use might be less prevalent than in the general population. The one consistent occupational hazard was a very high mortality from airplane crashes. The cumulative probability of dying in an aircraft accident reached as high as 1 to 3%.

A large study of U.S. Navy aviators evaluated the incidence of certain types of cancers based on hospitalizations within military hospitals (Hoiberg and Blood 1983). Rates of hospitalizations among 22,417 pilots were compared with over 110,000 non-pilot aircrew and other military personnel. While there were elevated hospitalization rates for certain types of cancers (Hodgkin's disease and testicular cancer), the incomplete nature of the follow-up as well as the possibility of increase surveillance for pilots because of their critical occupation limited interpretations. A higher rate of hospitalizations for dental problems among pilots was related to sports injuries and a keen sense of physical fitness.

In 1983, Milham published a proportional mortality study of death notifications within the state of Washington. Among pilots, rectal cancer was significantly elevated, based on six cases, whereas lung cancer was significantly below expectation and also based on six cases. Proportional mortality studies are of some value in generating hypotheses but they are susceptible to a variety of biases which limit their usefulness in hypothesis testing or making causal inferences. Proportional increase in one cancer, for example, might be related more to a deficit of some other disease than to a real increase in the cancer of interest.

The continued follow-up of a landmark epidemiologic study initiated in 1950's by Harold Dorn continues to provide information on smoking and occupational risks among United States veterans who served during World War I and World War II (Hrubec et al. 1992). In

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Table 3. Early studies of pilots and aircrew and statistically significant findings.

Study	Type	Significant findings	RR	Number cases
U.S. Navy's "1000 Aviator" cohort of WW II and Korean Conflict fliers (McIntyre et al. 1978)	Cohort, SMR	All cancer	0.35	16
		Cardiovascular disease	0.43	37
		All causes	0.46	95
U.S. Navy aviators, 22,417 pilots (Hoiberg and Blood 1983)	Cohort, comparing hospitalization rates with non-pilot aircrews and others	Elevated hospitalization rates for certain types of cancers, but details not provided.		
Washington state death notifications (Milham 1983)	PMR	Rectal cancer	4.4	6
		Lung cancer	0.4	6
		Aircraft accidents	>20	171
		Circulatory diseases	0.7	71
U.S. Veterans of WWI & WWII 1,358 pilots and navigators (Hrubec et al. 1992)	Cohort, internal comparison based on rates in other veteran occupations	Buccal cavity	4.2	3
		Colon cancer	1.5	17
		Other accidents	2.9	33
		Cardiovascular disease	0.7	170
		All causes	0.9	410
U.K. RAF, 12,416 who served abroad (Darby et al. 1990)	Cohort SMR and internal comparisons with other services: Royal Navy and Army	Stomach cancer	0.58	22
		Colon/rectum cancer	0.70	29
		Lung cancer	0.64	102
		Testis cancer	0.51	2
		Bladder cancer	0.43	5
		Prostate cancer	1.78	18
		All cancers	0.73	296
		Air accidents	47.6	68
		All non-cancer	0.72	784

the most recent publication, 1,358 pilots and navigators were evaluated and contrasted with other veterans within the overall study population of nearly 250,000 veterans, with rates adjusted for smoking. The number of events were relatively small, but cancer of the buccal cavity was increased significantly based on three deaths, and colon cancer was increased significantly based on 17 deaths. Deaths from airplane crashes were increased, and cardiovascular disease and all causes of death were in significant deficit. The authors noted that brain cancer and leukemia, which had been reported to be elevated in some studies of pilots, were not increased in this cohort study. One notable strength of this investigation is the good comparison group of veterans with other occupations. Nonetheless, pilots still appeared to be different and healthier than comparable military personnel. The study is limited due to small numbers.

The mortality experience of United Kingdom servicemen who served abroad in the 1950's and 1960's has been reported (Darby et al. 1990). Among 12,000 who served with the Royal Air Force (RAF) an extremely high mortality from air accidents (RR = 48) and a low mortality from diseases related to alcohol (RR = 0.48), such as cirrhosis of liver and alcoholism, was observed. Overall cancer occurred in significant deficit, as did cancers of the stomach, colon and rectum, lung, testis, and bladder. Hodgkin's disease (RR = 0.59) and leukemia (RR = 0.56) also occurred below expectation. Only prostate cancer (RR = 1.78) was significantly elevated. Servicemen in the Royal Navy had a similar increase in death due to prostate cancer (RR = 1.78). Officers had a lower risk of death from all cancers compared to enlisted men (RR = 0.73), and service in the RAF was associated with a significantly lower risk of death from all cancer (RR = 0.92) compared with service in the Royal Navy or Army.

RECENT STUDIES

Recent studies have been published of U.S. Air Force, Canadian, British, Finnish, and Japanese aircrew (Table 4).

Grayson and Lyons (1996a) evaluated cancer incidence among 59,940 Air Force pilots and aircrew based on hospitalization rates in military hospitals over the period of 1970 to 1989. A comparison with rates from the National Cancer Institute SEER (Surveillance Epidemiology and End Results) registries indicated a significant increase of all cancers (RR = 1.19), due in large part to elevations of skin cancer (both melanoma and nonmelanoma types). Bladder cancer was significantly elevated, and Hodgkin's disease was significantly in deficit. Comparisons with non-flying Air Force officers revealed a significant risk of testicular cancer among pilots.

In a case-control study of U.S. Air Force aircrew and non-flying officers, 230 brain cancers were identified

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and matched against 920 controls on the basis of age, race, and calendar year (Grayson and Lyons 1996b). The risk associated with being a pilot or aircrew member was significantly increased (RR = 1.77; 95% CI 1.2 to 2.7). However, when adjustment was made for military rank, which was taken as an indirect measure of socio-economic status, the association was reduced and was no longer significant (RR = 1.22; 95% CI 0.8 to 1.9). The authors stressed the importance of a good comparison group in studies of pilots and aircrew who have unique physical attributes, health habits, and avocations. Previously reported cancer risks, either high or low, might be related more to the inadequacies of a comparison group than to any association with flight. For example, the increase seen for melanoma and non-melanoma skin cancer might reflect the influence of lifestyle and excessive sun exposure from recreational endeavors. The elevated risk of brain cancer, unadjusted for rank, might be attributable to better diagnoses, surveillance, or other factors associated with higher social class.

CANADIAN STUDIES

Several studies have addressed health effects among Canada airlines pilots (Table 4). An early proportional mortality study suggested increased risks of brain and

Table 4. Recent studies of pilots and aircrew and statistically significant findings.

Study	Type	Significant findings	RR	Number cases
U.S. Air Force 59,940 aircrew (Grayson and Lyons 1996a)	Cohort, SIR cancer incidence comparing hospitalizations with SEER rates	All cancer	1.19	342
		Melanoma	1.50	49
		Non-melanoma skin	1.45	36
		Bladder cancer	2.09	19
		Hodgkin's disease	0.51	14
			RR	95% CI
U.S. Air Force brain cancer (Grayson and Lyons 1996b)	Case-control 230 cases and 920 controls, aircrew and non-flying officers	Unadjusted risk	1.77	1.2–2.7
		Adjusted for military rank	1.22	0.8–1.9
Canadian Pacific Airline pilots (Band et al. 1990)	Cohort, SMR 913 pilots	Rectal cancer	4.4	3
		Brain cancer	4.2	4
		Airplane accidents	21.3	23
		All causes	0.8	71
	Cohort, SIR Cancer incidence	Brain cancer	3.5	4
		Prostate cancer	3.9	3
		Non-melanoma skin	1.5	26
		Hodgkin's disease	4.5	3
Air Canada (Band et al. 1996)	Cohort, SMR 2,740 pilots	All cancers	0.61	56
		Lung cancer	0.25	8
		Aircraft crashes	26.6	31
		Circulatory diseases	0.60	81
		All causes	0.63	219
	Cohort, SIR Cancer incidence	All cancers	0.71	125
		Lung cancer	0.28	11
		Bladder cancer	0.36	4
		Rectal cancer	0.42	4
		Prostate cancer	1.87	34
		Non-CLL	1.88[a]	7
British Airways (Irvine and Davies 1992)	PMR Death notifications	All cancers	1.31	138
		Brain cancer	2.68	9
		Colon cancer	2.30	
		Prostate cancer	2.12	10
		Melanoma	6.68	6
		Aircraft crashes	115	36
British Airways (Irvine and Davies 1999)	Cohort, SMR 6,209 Pilots and 1,153 flight engineers	Only melanoma and plane crashes remained significantly elevated among pilots; only accidents among flight engineers.		
Japan Airlines (Kaji et al. 1993)	Cohort, SMR 2,327 aircrew	All causes	0.66	59
		Aircraft accidents	2.43	
Finnair cabin attendants (Pukkala et al. 1995)	Cohort, SIR Cancer incidence 1,764 flight attendants	Breast cancer	1.87	20
		Bone cancer	15.1	2

[a] (95% CI = 0.8–3.5).

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Table 5. Examples of low statistical power to detect radiation-induced cancer in two studies.

Characteristic	Air Canada pilots (Band et al. 1996)	Finnair flight attendants (Pukkala et al. 1995)
Number studied	2,740	1,764
Estimated annual equivalent dose	6 mSv	~2 mSv
Estimated cumulative dose	~100 mSv	15–20 mSv
Cancer of interest	Non-CLL	Breast cancer
Predicted radiation excess	0.15	0.10
Population expected occurrence	3.72	10.7
RR to detect	1.04	1.01
Study power	4%	1%

other tumors, although based on small numbers (Salisbury et al. 1991). In 1990, Band et al. published a report of 913 Canadian Pacific airline pilots using a straightforward cohort standard mortality ratio (SMR) analysis. Pilots were followed forward in time and cancer deaths counted and contrasted with that expected based on general population rates. Significant excesses were found for rectal and brain cancer as well as airplane crashes. Overall, there was a significant deficit of death from all causes taken together. Within the same population, cancer incidence was evaluated and contrasted with Canadian rates. Brain cancer was elevated as was prostate cancer, non-melanoma skin cancer, and Hodgkin's disease. Prostate and non-melanoma skin cancer might be related to the more frequent and intense surveillance that is afforded pilots in contrast to the general population.

In 1996, a larger study of 2,740 Air Canada pilots was published using similar methodologies (Band et al. 1996). There was a deficit for all cancers, and lung cancer in particular, suggesting that pilots may smoke and use tobacco products less frequently than persons in the general population. A very high risk of death due to airplane crashes was seen, and large deficits occurred for circulatory disease and all cause mortality. A cancer incidence evaluation found that all cancers were in deficit by about 30%, notably lung, bladder, and rectal cancer. Prostate cancer was significantly elevated as was acute myelogenous leukemia; non-chronic lymphocytic leukemia (non-CLL) was elevated but not significantly (RR = 1.88; 95% CL = 0.8 to 3.5).

The authors of the Canadian study (Band et al. 1996) discussed the low statistical power to detect an effect of cosmic rays within their series (Table 5). They estimated the annual equivalent dose received by the pilots as 6 mSv and used models of radiation-induced non-CLL (NAS/NRC 1990) to predict an excess of 0.15 cases due to radiation. This was contrasted with a population expected value from other nonradiation causes of 3.72. Thus, the RR of possible radiation-induced leukemia to be detected was a tiny 1.04. The statistical power to detect such a small risk was about 4%, i.e., far below the nominal power of 80% commonly used as a guideline for conducting an epidemiologic study. Even if the sample was 10 or a 100 times larger, the very low risk predicted from the radiation dose received would still not be detectable by epidemiologic means.

Three recent studies from Denmark (Gundestrup and Storm 1999), Norway (Haldorsen et al. 2000), and Iceland (Rafnsson et al. 2000) report significant increases in malignant melanoma but all authors attribute this to excessive sun exposure during leisure time activities.

BRITISH AIRLINES

Another series of studies involved pilots and flight engineers for British Airways (Table 4). An early study applied the proportional mortality ratio approach based on death notifications (Irvine and Davies 1992). This approach might provide hints of possible health hazards but is not adequate for concluding causality. For over 400 deaths occurring between 1966 and 1989, the proportional mortality ratio for all cancers was 1.31 based on 138 cancers. Cancers of the brain, colon, and prostate as well as melanoma were significantly elevated. Death due to airline crashes was also proportionately high based on 36 deaths. A more powerful cohort study was later conducted and included pilots and flight deck engineers. The earlier suggested increase for all cancers was no longer present, and only malignant melanoma and aircraft accidents remained significantly elevated among pilots and only accidents among flight engineers (Irvine and Davies 1999). The excess of melanoma might reflect lifestyle factors associated with increased sun exposure from recreational activities. It is also possible that elevations in prostate cancer might be related to increased surveillance and screening afforded pilots because of the requirement for frequent physical examinations.

JAPAN AIRLINES

For completion, a study of over 2,300 Japan Airline aircrew indicated a significantly low risk of deaths from all cancers based on 59 cancers, and a very high risk of death due to airplane crashes (Kaji et al. 1993). This study was based on a relatively small number and individual cancer sites were not evaluated.

FINNISH AIRLINES

A comprehensive study of flight attendants was conducted among Finnair employees (Pukkala et al. 1995). Over 1,700 cabin attendants, predominately female, were evaluated using cancer registry linkage techniques. A significant excess of bone cancer was reported but based on only two recorded cases and attributed to chance. Leukemia and melanoma were not significantly elevated.

A significant risk of breast cancer, however, was recorded based on 20 incident cases (RR = 1.87, 95% CI = 1.15 to 2.23). The authors estimated the annual equivalent dose to be approximately 2 to 3 mSv and the mean cumulative equivalent dose to be approximately 15

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to 20 mSv, i.e., an extremely low career dose. Based on this cumulative dose, the expected RR of breast cancer from radiation would be a tiny 1.01—and not within the realm of epidemiology to detect (Table 5). This suggests that factors other than or in addition to radiation were likely associated with the significant increase in breast cancer seen among the Finnish flight attendants. The authors, in fact, evaluated social class and reproductive factors and concluded that these characteristics could account for a portion of the increased risk of breast cancer seen among the flight attendants in comparison with the general population. Preliminary results indicate that the risk of breast cancer has remained elevated in extended follow-up, although the reasons for the excess remain unclear.

There were several inconsistent patterns in the data. For example, while risk of breast cancer was more pronounced 15 and more years after first employment, there was no apparent trend by number of years worked, i.e., there was little evidence of a dose response using years worked as an indirect measure of cumulative cosmic-ray exposure. One author recently concluded that "the results suggest an increased risk of breast cancer among flight attendants but give little information regarding its etiology" (Auvinen 1998).

A subsequent Danish study of 915 flight attendants was reported in a letter to the editor that was generally consistent with an increase in breast cancer, although the increase was not significant. There was no elevated risk for bone cancer or leukemia (Lynge 1996).

A significant increased incidence of breast cancer has been observed in studies of western women exposed to fractionated radiation, albeit low-LET. Studies of young women undergoing multiple chest x-ray fluoroscopies in the United States, for example, indicate that approximately 2,000 mSv would be required to produce a RR of 1.87 (Boice et al. 1991), i.e., the risk observed in the Finnish study. Such a large cumulative dose would not be possible even from frequent air travel over many years. The 95% confidence intervals around the Finnish flight attendant RR of 1.87 was 1.15 and 2.23, which would suggest a possible exposure range of 400 to 3,000 mSv if radiation were the likely responsible factor. Since such career doses are not possible, this suggests that flight attendants are likely different from the general population used for comparison and that they might possess characteristics (such as delayed childbirth) that increase their risk of breast cancer.

What is the magnitude of breast cancer risk factors associated with common reproductive characteristics? In a recent study of x-ray technologists who received multiple exposures to ionizing radiation during the course of their employment, reproductive and familial risk factors were more important than low-dose radiation exposure (Boice et al. 1995). The RR of nulliparity was 1.39, and the RR of having a first child after the age of 30 was 1.4. The RR associated with having an early menarche before the age of 11 compared to after the age of 15 was 1.89. The RR of breast cancer associated with having a first degree relative with breast cancer (i.e., a positive family history) was 2.0. These RRs can be contrasted with the presumed RR of breast cancer from 100 mSv of flight crew exposure of approximately 1.04. Studies of aircrew have low statistical power and epidemiology will have a difficult time trying to discern radiation effects from the effects of other factors.

Table 6. European study on cancer risk among airline pilots and cabin crew (Blettner et al. 1998; International Workshop 1998).

Country	Cockpit	Cabin Crew
Denmark	2,400	5,000
Finland	750	2,000
Germany	6,000	20,000
Greece	600	1,000
Iceland	460	>1,000
Italy	2,200	4,900
Netherlands	5,000	10,000
Norway	3,800	3,600
Sweden	1,500	3,000
Total	22,500	50,000

ONGOING STUDIES

A workshop sponsored by the Medical University of South Carolina in February 1998 summarized a large number of ongoing epidemiologic investigations of pilots, flight engineers, aircrew and flight attendants (International Workshop 1998). Studies are being conducted in California, Germany, Finland and other Scandinavian countries (the Nordic study), Italy and England, and there is a newly initiated European study (Table 6). Mortality among US commercial pilots and navigators is also being studied (Nicholas et al. 1998).

In a comprehensive study of female flight attendants sponsored by the National Institute for Occupational Safety and Health, the Federal Aviation Administration, the U.S. Department of Defense, and the National Cancer Institute, measurements are being made of the cabin air environment, which will provide information on air pollutants that might be related to disease risk (International Workshop 1998). The changes to hormone levels and menstrual characteristics are also being measured.

Overall, approximately 80,000 aircrew are currently being studied, but the low-cumulative exposures and limited dose range still may not be sufficient to discern any low-level radiation risks. The long latency associated with radiogenic solid tumors is also problematic and indicates the need, if desirable and feasible, for long-term follow-up. Another challenging epidemiologic issue is that risk is not maximal with regard to the time from first exposure but likely related more to the time from last exposure when sufficient exposure has been accumulated. Computations taking account of changing ages at exposure and ages at risk patterns (and different latency intervals) are not as simple conceptionally as those for acute (brief) exposures.

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Table 7. Epidemiologic issues in studies of aircrew exposed to increased levels of natural background radiation from cosmic rays.

- Bias (healthy worker effect)
  Adequacy of comparison population
- Confounding (risk factors other than cosmic rays: Table 2)
- Chance
  Low statistical power associated with low doses (lifetime cancer risk of career dose of 100 mSv about 5×10^{-3} of natural risk of about 250×10^{-3})
- Exposure assessment and assumptions
  - Altitudes
  - Definitions of flight hours (gate to gate time overestimates exposure)
  - Routes (polar, equator)
  - Calendar period (solar flare activity)
  - Return flights (non-occupational)
  - Validity of neutron assumptions with regard to biological effectiveness to cause cancer in humans, i.e., does the W_R used for radiation protection have biological value in an epidemiologic context.

CONCLUSION

Pilots and aircrew are a unique occupational group which until recently has not been well studied. Studies to date have revealed no clear picture with regard to disease patterns, except a low risk of total deaths in comparison with the general population and a high risk of death from airplane accidents. A career dose of 100 mSv might be obtained among aircrews flying at high altitudes. The presumed increased risk of death due to cancer over a lifetime from 100 mSv is approximately 0.5% (NCRP 1993) to be contrasted with the 25% lifetime risk of cancer deaths from all other causes.

Conducting epidemiologic studies of aircrews is problematic because of the potential for bias, confounding, and the play of chance (Table 7). Bias is related to the healthy worker effect, which points to the importance of an appropriate comparison group. Confounding is related to other occupational or lifestyle factors (Table 2) that could produce misleading results if not accounted for. Chance is related to the low career dose and associated low statistical power to detect an increase in cancer risk. Exposure misclassification is related to difficulties in estimating career dose as well as the biological value of neutron weighting factors in an epidemiologic context.

Nonetheless, aircrews experience a variety of interesting exposures and possess particular characteristics that support the need for further investigation. Reported increases in some cancers such as melanoma and breast cancer, for example, should be clarified, and it is interesting that excess chromosome aberrations among pilots and aircrew have been reported in some studies (Romano et al. 1997). Ongoing studies should provide information on the possible range of risks associated with a flying occupation as well as dissect the contributing components of risk, including cosmic radiation.

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